CARCINOMA OF THE APPENDIX WITH METASTASIS TO THE ILEOCOLIC GLANDS.*

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THE subject of carcinoma of the appendix has been extensively reviewed by my colleague, Dr. Harte, and it is clear that the diagnosis of this disease, when limited to the appendix, cannot be made before operation. Even after operation the pathologist is generally the first to discover its presence in an organ removed for other causes. In the majority of cases the disease seems to be entirely confined to the appendix, and the removal of that organ brings about a cure. In a few cases, however, microscopical examination reveals that the disease has gone beyond the appendix, and these cases are of special interest to the surgeon, for they compel a second more or less dangerous operation. I desire to report a case of this type in which the primary growth in the appendix had spread to the cæcum and presented metastases in the ileocolic glands.

A. B., aged 21; female; single; white; American. The family history was negative, except that many members were rheumatic, the patient herself being a frequent sufferer. She had had most of the diseases of childhood, including scarlet fever followed by nephritis. From the age of eleven, that is, for ten years, she had had repeated attacks of sharp pain, localized in the right iliac fossa, sometimes with chilly sensations and slight fever, at other times with no disturbance of temperature. The sharp pain would last from a few hours to a day or two, and subside with a feeling of soreness. These attacks were usually attributed to some indiscretion in diet.

April 20, 1907, the patient was seized with violent pain in the appendix region while at dinner; the pain was so severe that she almost fainted. She had chilly sensations and felt slightly feverish; had nausea but no vomiting. After a couple of hours the pain lessened in severity and was followed by a feeling of discomfort and soreness in the right iliac region. During the next five days she had several slight attacks of this colic. I saw the patient in consultation with Dr. Henry C. Earnshaw four days after the onset of the attack.

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Physical Examination.—Thin but not emaciated; color good; slight lateral curvature of spine. Chest negative. Temperature and pulse normal. Abdomen retracted; no rigidity; slightly tender mass the size of a hickory-nut palpable in appendix region. Cæcum distended with gas. Urine contained a trace of albumin but no casts. There was some anæmia: R. B. C., 4,264,000; Hb., 75 per cent.; leucocytes 8,600. Operation was advised and accepted.

April 27, 1907, the abdomen was opened through a gridiron incision and the palpable mass was found to be an intussusception of the appendix into the head of the cæcum. About an inch of the tip of the appendix was visible beyond the cæcal margin. The portion within the cæcum was almost round and nearly an inch in diameter. It felt like an inflammatory mass and was thought to be due to the chronic condition of the intussusception. The portion of the cæcum containing this mass was resected and the opening closed with Lembert sutures. A small pin-head sized pearly mass was noticed on the cæcum an inch beyond the area resected, but at the time of operation nothing was thought of it. The ileocolic glands were somewhat enlarged. The abdomen was closed with layer sutures and the recovery was uneventful. The patient was discharged from the hospital May 11, 1907, in good condition, weighing 116 pounds.

The examination of the specimen was made by Dr. Warfield T. Longcope, Director of Ayer Clinical Laboratory, and the findings confirmed by Prof. Allen J. Smith, of the University of Pennsylvania.

Pathological Report.—The specimen consists of a portion of the cæcum and the appendix. The major portion of the specimen consists of a rounded, mulberry-like mass, 2½ cm. in diameter, which has a mottled red and yellow surface. This is said to be the mucous membrane of the colon, though it has lost all resemblance to normal mucous membrane.

Towards the middle of the specimen there is a collar-like contraction and the colon surface forms a little frill about it. Coming out from this collar is the tip of the appendix which forms a curved bulbous knot about 2 cm. in length and 1 cm. in diameter. The surface is fairly smooth and white. Here and there are a few yellow pin-point nodules. It has a cystic feel. When it is opened a thick buttery material escapes. The lining is thick, opaque and white. The lumen can readily be found, and a probe passes into it from the colon and out through the most prominent portion of the main mulberry-like mass. Evidently there is a partial invagination of the appendix in the colon.

Sections are made through the tip of the appendix. It has been opened. Instead of the mucous membrane there is an irregular growth of cells arranged in more or less solid alveoli. The spaces filled with cells are separated by a moderate amount of connective tissue stroma. The cells forming these nests are oval, regular, and contain quite deeply staining round nuclei. The protoplasm is poorly made out. No karyokine figures are seen. Here and there a space is seen lined by high columnar epithelium filled with mucus. They resemble the normal crypts of the appendix. The growth is seen extending down into the submucosa and infiltrating the muscular coats. The small nodule on the external aspect of the appendix is composed of a growth like that of the appendix itself.

When it was discovered that the appendix was the seat of a carcinomatous growth, sections were made through the portion of the appendix invaginated in the cæcum and through the wall of the cæcum itself. The sections present a curious appearance. The sections in general show four definite zones. A central cellular area, a wide zone of smooth muscle, beyond which is a second cellular zone covered by the fourth zone formed by the mucous membrane of the colon. In the centre corresponding to what should be the lumen and mucous membrane of the appendix, is a solid growth of small polyhedral cells arranged in large spaces separated by a delicate or fairly thick connective tissue stroma. Surrounding this central growth is a wide circular band of smooth muscle which evidently represents the muscular coats of the appendix and cæcum. In some sections this band is complete and unbroken, while in others it is infiltrated more or less extensively with the cells of the growth. Outside of the smooth muscle ring is the second cellular zone, which evidently takes the place of the submucosa of the colon. This zone is quite wide and is made up almost exclusively of irregular solid masses of cells of the new growth, which are separated by a connective-tissue reticulum. In many places this growth in the submucosa is separated from the mucosa definitely by the muscularis mucosa. The mucosa itself looks thin, the crypts are not numerous, and the stroma is filled with small round cells. In other sections the muscularis mucosa has been destroyed and there is direct connection between the growth in the submucosa and the mucous membrane.

In a few places in the sections comparatively normal crypts of Lieberkühn are seen, but usually replacing the crypts there are irregular tortuous spaces, extending from the surface into the solid growth below, which are partially or entirely filled with the polyhedral cells forming the new growth. The stroma between is œdematous and infiltrated with polymorphonuclear leucocytes, small round cells and epitheloid cells.

Such sections suggest that the growth may have originated from the glands of the mucous membrane of the cæcum, but it is difficult to say whether the growth extends down from the mucosa or up from the more extensively involved submucosa. From the fact that the entire appendix, even to its tip, is the seat of a growth, and from the fact that the mucous membrane of the colon shows a new growth in only one or two places where there is a direct connection between the growths in the submucosa, it seems reasonable to suppose that the carcinoma arose from the appendix and involved the cæcum by direct extension of the growth.

Diagnosis.—Carcinoma arising in the appendix. Invagination of appendix into cæcum with extension of growth to that portion of cæcum which surrounds the appendix.

The pathological findings were fully discussed with the father of the patient, and after some delay a second operation was agreed to.

June 11, 1907, an incision was made through the right rectus muscle, and the cæcum with three or four inches of the ileum was resected, including the entire group of ileocolic glands. A lateral anastomosis was made with rubber-covered clamps and Pagenstecher thread. As the mesenteric vessels were ligated as near the back as possible, there was a slight hemorrhage from one of the vessels before it was secured with forceps. This deep removal of the mesentery was done to insure the complete removal of the ileocolic glands. The wound was closed without drainage.

For 48 hours after operation the patient was quite ill, with vomiting, distention and signs of intestinal paresis. The bowels were finally moved, the vomiting ceased, and from then on the recovery was uneventful.

The patient left the hospital at the end of three weeks weighing 113 pounds. Two months after the operation her weight had increased to 121 pounds, and March 1, 1908, her weight was 129 pounds. Her best weight previous to these operations had been 132 pounds. She is apparently in perfect health.

Second Pathological Report.—The specimen consists of the cæcum and about 10 cm. of the ileum. The ileum to the right of the specimen is bound by adhesions to the cæcum. The line of junction is covered by a delicate film of connective tissue. The point of excision of the invaginated appendix is entirely hidden. At the point where the ileum and cæcum are adherent there are, deep down, firm adhesions. A number of the ileocolic glands and the mesentery are included in the specimen. On opening the intestine a thick, yellowish-green material escapes from the ileum. The cæcum is filled with the same material. The mucous membrane looks pinkish, soft and apparently normal. In the deepest part of the cæcum is a dimpled scar in which one sees a stitch. At the base of this point the cæcum and ileum are adherent and the adhesions, though not extensive, feel hard. The mesenteric lymph-nodes vary from 0.5 to 1.5 cm. in diameter. They are regular but quite firm and white. On section some of them show small whitish points along the periphery.

Microscopical Examination.—Sections are made through the adhesions at the seat of operation, through the ileum and colon above and below the seat of operation and through eleven of the mesenteric lymph-nodes. *At the seat* of the operation the section includes a few of the stitches. The subperitoneal surface of the colon and ileum are adherent. Between these surfaces there is a little blood, fibrin and granulation tissue. There is a general infiltration with small round cells, epithelial cells, plasma cells and a few polymorphonuclear leucocytes. About the remains of the stitches there are many foreign body giant cells. The mucous membrane of the colon and the ileum is slightly œdematous. The lymphoid follicles are greatly swollen and the germinal centres show hyperplasia. In the mucous membrane of the ileum, and especially of the colon, there are great numbers of eosinophiles. There are no evidences of tumor growth.

Sections through the colon and ileum below and above the operation wound appear normal except for swelling of the lymphoid tissue. *All the mesenteric lymph-nodes* show some swelling of the lymphoid tissue with some endothelial proliferation. Many of the lymph sinuses are dilated. Occasionally they contain many lymphoid cells. In two of the lymph-nodes metastases are found. They lie in the peripheral sinuses, localized fairly well in one position. In one gland the metastases also extend into the sinuses surrounding one follicle. The cells have a gland-like arrangement, suggesting very closely the structure of the original growth. The cells are columnar or cuboidal, and lie in columns and rows. The protoplasm is granular and the nuclei oval and pale. A few karyokinetic figures are seen.

Diagnosis.—No return of growth found at seat of operation. Metastases to two mesenteric lymph-nodes.

The second operation seems to have been fully warranted by the metastases found in the ileocolic glands, and the judgment of the two pathologists who examined the specimen in urging a second operation proved correct. While it was rather anticipated that we would find in the cæcum areas of malignancy, particularly at the pinhead-sized pearly spot which was noticed at the time of the first operation, yet a careful examination of all the tissue removed failed to reveal any malignancy except in the mesenteric glands.

The sequence of events in this appendix might be explained in two totally different ways: First, that the epithelial growth was of the character of the small benign tumors sometimes found in different parts of the intestinal tract, and which may be present for long periods of time with very slow growth. Such a tumor through the slow formation of fibrous tissue may have drawn the appendix within the cæcum, and after the growth had invaded the walls of the cæcum through extension, metastasis to the ileocolic glands followed. In other words, the tumor may have been practically local and latent until the cæcum was invaded, when its malignant characteristics developed.

Second, that the appendix had been the seat of long-standing chronic disease which recently had undergone malignant change, the operation uncovering it in its early stages. The pathologists, I believe, would rather favor the first view expressed.